## REMARKS

### I. Status of Claims.

This application has been reviewed in light of the Office Action dated January 23, 2002. Claims 1-15 are presently pending. Applicants have added new claim 16 to further emphasize their invention. Claims 1, 4, 7-9, 11 and 14 are amended in a manner that is believed to overcome rejections contained in the pending Office Action. No new matter or issues are believed to be introduced by these amendments. Support for the amendments is found throughout the specification and drawings.

### II. Objection to Oath or Declaration.

The Examiner in the official office action dated June 13, 2002 objected to the oath or declaration as not being in compliance with 37 CFR 1.67 (a). Examiner again makes note of the defection Oath or Declaration. Applicants submitted a new oath and declaration in compliance with 37 CFR 1.67 (a), on January 13, 2003 and would respectfully submit that this objection has been overcome.

### III. Information Disclosure Statement.

The Examiner objected to the Information Disclosure Statement (IDS) filed on June 12, 2002 stating that the cited references have not been found to date. Applicants have attached to this response PTO-form 1449 along with copies of those references unsigned by the Examiner.

**IV. Claim Objections.**

The Examiner objected to claims 9, 11 and 14 due to informalities in the claim structure. Applicants have amended these claims as suggested by the Examiner to correct these informalities. Applicants thank the Examiner for her suggested amendments and diligence in the examination of the instant application.

**V. Claims 11-13 rejected under 35 USC 112 first paragraph.**

The Examiner rejected claims 11-13 under 35 USC 112, first paragraph stating that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make an/or use the invention commensurate in scope with these claims. Applicants respectfully traverse this rejection.

The Examiner states that the specification has not demonstrated the use of the tetrapeptide Gly-Pro-Val-Pro-Ch2($N^+$CvH5)Cl in treating diabetes mellitus. The Applicants would respectfully suggest that under the provision of 35 USC 112, first paragraph it is not required that Applicants demonstrate the use of a compound. The written description requirements generally require Applicants to provide an enabling description of the invention to one of ordinary skill in the art. The CCPA has stated that "[n]ot every last detail is to be described, else patent specification would turn into production specifications, which they were never intended to be." In re Gay, 309 F.2d 769, 135 USPQ 311, 316 (C.C.P.A. 1962). Applicants must merely provide sufficient detailed as to allow a person skilled in the art the ability to practice the invention. This they have done.

The Examiner further states that claims 11-13 encompass a method of treating disorders in mammals, and that the scope of claim 1 would have included genetic disorders, the treatment of which is not described so as to enable the scope of the claim. Applicants would respectfully submit that contrary to the Examiner's assertion, claim 11 is limited in scope to "[a] method of treating disorders in mammals that can be treated by modulating the DP IV enzymatic activity of a mammal". Thus by operation of this limitation those disorders for which modulation of DPIV enzymatic activity has no effect would be excluded. The scope of claim 11 and its dependent claims is limited to those metabolic disorders that will respond to a modulation in enzymatic activity of DP IV.

There are numerous instances in the prior art which describe how modulation of DPIV activity can influence various disease states. For Example, Applicants have cited in the specification DE 196 16 486, which discloses that "by means of DP IV inhibitors it is possible to prevent or alleviate metabolic anomalies, such as excess weight, glucosuria, hyperlipidaemia, and possible serious metabolic acidosis and diabetes mellitus, which are the result of prolonged elevated glucose concentrations in the blood" (Specification page 2 lines 3-6). This is not what Applicants are claiming. Rather Applicants claim a method of treating metabolic disorders in mammals that can be treated by modulating the DP IV enzymatic activity by "administering to said mammal a therapeutically effective amount of a compound of the general formula A-B-C, wherein A is an amino acid, B is a chemical bond between A and C or is an amino acid, and C is an unstable inhibitor of DP IV said unstable inhibitor is a dipeptide compound having a C-terminus with an active carbonyl group wherein said unstable inhibitor does not contain a boronate, phosphonate or trifluoroalkyl ketone group". This claimed subject matter, however, is not made obvious by the prior art.

The Examiner additionally states that Applicants have not indicated the treating conditions such as the dose, method of administration and the effect of the compound. Applicants would respectfully suggest that it has disclosed within the specification a method of administration. (see specification page 5 line 5-7), dosing (see specification page 8 line 32-33; page 9 line 14-18) and the effect of the compound (see specification page 5 lines 8-11). Claim language must be read in light of the specification as it would be interpreted by one of ordinary skill in the art. In re Moore, 58 CCPA 1042, 1046-1047, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (1971). Applicants would respectfully submit that it has more than met the requirements of 35 USC 112 for claims 11-13 and would therefore respectfully request that this rejection be withdrawn.

**VI. Claims 1-15 rejected under 35 USC 112, second paragraph.**

The Examiner rejected claims 1-15 as being indefinite because of the term "a dipeptide derivative". The Examiner states that it is unclear how different the derivative is from the parent compound. It has been suggested by the Examiner that Applicants use "compound" rather than "derivative" as presently claimed. Applicants thank the Examiner for this suggested amendment and have amended the rejected claims to reflect Examiner's suggestion.

Applicants would respectfully submit that such amendments are merely to make explicit what is implicit within the pending claims. Applicants would further submit that the substitution of "compound" for "derivative" is to more clearly define Applicants' invention and does not in any way change the breadth or scope of the pending claims. In light of these amendments, Applicants would respectfully request that this rejection be withdrawn.

The Examiner further rejected claim 4 under 35 USC 112 , second paragraph because it is not clear what the terms "Thia" and "Pyr" mean. Applicants would respectfully submit that "Thia" denotes "thiazolidine", which is a mimetic of the amino acid proline and "Pyr" denotes pyrrolidine. Applicants would respectfully submit that these denotations are commonly accepted and understood by those skilled in the art and therefore would respectfully request that this rejection be withdrawn.

Further rejection under 35 USC 112, second paragraph was made regarding claims 11-13. The Examiner states that the claims as presented lack the omitted steps of the effective amount of the compound used and the method of administration and the outcome for the treatment. Applicants have amended claim 11 to more clearly define the claimed method requiring that a therapeutically effective amount of the compound be administered. As set forth in the specification, a distinct advantage of the instant invention is that each organism will release the exact amount of inhibitor that is necessary to inhibit the amount of DP IV that is present, which is different in individual cases. If for example a patient has a high concentration of DP IV then a large amount of inhibitor will be released, if there is only a slightly elevated concentration of DP IV, only a small amount of inhibitor will be released. Applicants respectfully suggest that claims 11-13 as amended meet the requirements of 35 USC 112 in light of the specification and would therefore respectfully request that this rejection be withdrawn.

The Examiner also rejected claim 14 under 25 USC 112, second paragraph as having an insufficient antecedent basis for "dipeptide cyanide", because dipeptide cyanide does not contain an active carbonyl group. Applicants have amended claim 14 to overcome this rejection. Applicants have further added claim 16 to further emphasize their invention. Support for added

claim 16 can be found generally throughout the specification and claims, with particular reference to page 8 line 17.

**VII. Rejection of Claims 1-3, 5 and 8-12 under 23 USC 102(b)**

The Examiner rejected claims 1, 8-12 and 15 under 35 USC 102 (b) as being anticipated by Bachovchin et al. WO 93/08259 (Bachovchin). The Examiner states that Bachovchin discloses an inhibitory compound of DP IV having a structure of Group I-Group II, where Group I contains unblocked peptide, and Group II contains a boronate, a phosphonate or a trifluoroalkyl kentone group. Applicants respectfully suggest that the claims as amended are no longer anticipated by Bachovchin and would therefore respectfully request that this rejection be withdrawn.

**VIII. Rejection of Claims 1, 8-12 and 15 under 35 USC 102(b).**

The Examiner rejected claims 1-3, 5 and 7-11 under 35 USC 102 (b) as being anticipated by Bachovchin et al. WO 95/11689 (Bachovchin). The Examiner states that Bachovchin discloses compounds containing dipeptides with a fluoroalkyl ketone group and therefore the rejected claims are anticipated by the reference. Applicants respectfully suggest that the claims as amended are no longer anticipated by Bachovchin and would therefore request that this rejection be withdrawn.

**IX. Objection to claim 8.**

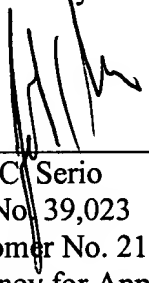
Objection was made to the present form of claim 8 as not being the usual way of describing a pharmaceutical composition. Applicants have amended claim 8 as suggested by the

Examiner. Applicants thank the Examiner for this suggested amendment and her diligence in the examination of the instant application.

## CONCLUSION

Applicants respectfully request expeditious consideration and passage of the present application to issuance. The Examiner is invited and encouraged to telephone the undersigned if she believes such would facilitate prosecution of the present application.

Respectfully submitted,



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